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10/523,312	10/25/2005	Stephen Berezenko	063572-5001US	7926

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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	**PAPER NUMBER**
1656	

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03/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,312	BEREZENKO ET AL.	
	Examiner	Art Unit	
	AGNES B. ROOKE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-21* is/are pending in the application.

4a) Of the above claim(s) *11,12,14,16-18 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/26/2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *March 16, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-10, 13, 19, and 20 in the reply filed on 12/03/2007 is acknowledged. Claim 13 would be examined in part in regards to an elected invention, i.e. mutant human albumin.

Examiner contacted Mr. David Owens on February 21, 2008, to inform the Applicants that claim 13 would be examined in part only in reference to the human serum albumin, and not in reference to a nucleic acid sequence or an expression cassette. Mr. Owens agreed that claim 13 would be examined in part and elected invention of Group I. See the updated Restriction below.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-10, 13 in part, 19 and 20, drawn to isolated mutants of serum albumins.

Group II, claim(s) 11, 12, 13 in part, 17, 18 and 21, drawn to isolated nucleic acids encoding mutants of serum albumins methods of obtaining mutant serum albumins by using the nucleic acids expressing said mutants.

Group III, claim(s) 14, drawn to a cell culture medium comprising a mutant serum albumin.

Group IV, claim(s) 16, drawn to a method of altering growth characteristics of a cell in cell culture by culturing cells in the presence of a mutant serum albumin.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Carter (W0 2002/05645 – cited on IDS from 03-16-2006) discloses a modified serum albumin in which the affinity to trace metals such as nickel and/or copper is reduced or eliminated. The modified serum albumin is either truncated by at least one amino acid at its N-terminal end or is mutated in such a way as to disrupt the metal binding site of the serum albumin binding site VI. Mutations to this binding site include elongation, insertion or other changes to the N-terminal end, such as to the histidine at amino acid position 3, which either sterically hinder the binding site VI or eliminate vital binding interactions, and thus reduce the affinity of this region to metals such as nickel or copper (see p. 7, lines 10-23 and p. 9, lines 5-16).

Therefore, the technical feature linking the inventions of Groups I-IV does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not differentiate the claimed subject matter as a whole over the prior art. Since according to PCT Rule 13.2 the presence of such a common or corresponding special technical feature is an absolute prerequisite for unity to be established, and given that there does not appear to be any other technical feature common to the claimed subject matter as a whole which might be able to fulfill this role, the currently claimed subject matter lacks unity of invention according to PCT Rule 13.1.

Claim Disposition

Claims 1-14 and 16-21 are pending. Claims 1-10, 13, 19, and 20 were elected. Claim 15 is cancelled. Further, claims 11, 12, 14, 16-18, and 21 are withdrawn from further consideration pursuant to 37 CFR 1.12(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Thus, claims 1-10, 13, 19, and 20 are examined.

Priority

This application is a 371 of PCT/GB03/03199 filed on 07/28/2003 that claims foreign priority to United Kingdom 0217347.4 filed on 07/26/2002. The priority is awarded to these documents.

Drawing

The Drawings submitted on 01/26/2005 are accepted by the examiner.

IDS

The Information Disclosure Statement filed on 03/16/2006 is signed by examiner and the copy is provided with the instant office action.

Objection to Specification

1. Specification is objected to because of the following informalities:

   a) On page 6 and 7 of the specification the mutations designated with an arrow should be re-written in the text form.

b) The specification on page 35 is objected to because the inserted Table is not in a proper form. Examiner suggests that the Table, as disclosed, should be made into a figure.

c) On page 14, the description of Figure 1 mentions highlighting, but none is visible in the poor quality drawing. Correction of the drawing or of its description is required. Additionally, the descriptions of Figure 3c and 8 mention color but none is found in the drawing. Additionally, in Figure 14, sections a-e mentioned in the description are unclear in the drawing. In Figure 16, sections a-b are unclear. The 2 panels in Figure 15 are unclear.

Thus, proper correction of the above is required.

Objection to Claims

2. Claims are objected to because of the following informalities:

a) Claim 1 is objected to for improperly punctuating the sequence identifier. The proper sequence numbering is "SEQ ID NO:1" without the extra period. Additionally, the writing out of the sequence of SEQ ID NO:1 is unnecessary and may be removed by amendment.

b) Claim 8 is objected to because it does not follow the proper form, since the arrow used in reference to particular mutations should be deleted and the claims should be re-written in the text form, for example: 'wherein X1 is any of A, F, G,..." and so on.

c) Claim 10 is objected to because the spacing between “Asn” and "99His" should be deleted.

d) Claim 2 is objected to because the phrase "*physiological characteristics are a change in cell adhesion to a substrate, percentage viability of cell, or cell growth of cells in culture”* should be re-written to indicate that the physiological characteristics are caused by the change in the polypeptide claimed, or that the changes are caused in the cells because the peptide is administered to the cells.

Thus, proper correction of the above is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-10, 13, 19, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 1, 3, and 19 are indefinite because due to the phrase “displays an altered metal binding affinity or one or more physiological characteristics with respect to native human serum albumin”, it is not clear whether the physiological characteristics with respect to a native human serum albumin are altered or not; in other words, does the "or" join two altered things does does the “or” join “altered metal binding affinity” and “physiological characteristics”. Thus, further definition of those characteristics is required in the claims as presented.

Examiner suggests that the claim be amended to state “said mutant displays an altered metal binding affinity or an altered physiological characteristic with respect to native HSA.”

b) Claim 3 is indefinite because it refers to a “Table 1.” See MPEP 2173.05(s) Reference to Figures or Tables: Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted).

c) Claims 1 and 3 are indefinite because the phrase “substantially comprising” in reference to an isolated mutant serum albumin does not reflect the percent of identity of the mutant to the native peptide since one skilled in the art would not know whether “substantially” represents 65% or 75% or 80% identity to the native peptide, and the term “substantially comprising” can also refer to any fragment of the mutant serum albumin, for example. Therefore, further specification of the identity of SEQ ID NO:1 is required. All dependent claims 1, 4-9, 13, 19, and 20 are included in this rejection because they do not cure deficiencies of claims 1 and 2.

d) Claim 4 is indefinite because nowhere in the claims or in the disclosure the native sequence of human serum albumin is defined. Thus, it is impossible to clearly defined 90% identical sequences, for example.

e) Claim 5 is indefinite because the phrase "substantially similar in terms of general overall folding" with respect to the native serum albumin does not specifically disclose what folding is at issue, for example, and whether it involves beta-sheet of alpha-helix, and how similar is substantially similar? Thus, further specification in the claim is required.

f) Claim 10 is indefinite because a mutant of human serum albumin is claimed with a mutation of Asn99His, Asn99Asp, or His67Ala, however there is no SEQ ID NO assigned to such a mutant and one skilled in the art would not known where a desired position for such mutation is present and where the sequence ends or starts, for example. Thus, SEQ ID NO should be assigned to such a mutant.

g) Claim 13 lacks clear antecedent basis to claims 1 or 3 because claims 1 and 3 refer to a mutant mammalian serum albumin protein and claim 13 refers to "a nucleic acid sequence or an expression cassette." Therefore, the non-elected limitation should be deleted to render claim 13 as definite.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10, 13, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant invention is directed to an isolated human serum albumin substantially comprising SEQ ID NO:1 or human serum albumin with other mutations.

The instant specification does not describe all possible human serum albumins that substantially comprise SEQ ID NO:1 or mutated human serum albumin with other mutations and/or other functions. Therefore, the aforementioned claims lack adequate written description.

Accordingly, in the absence of sufficient recitation of identifying characteristics, the specification does not provide adequate written description of the claimed genus of such group of proteins, i.e. mutated human serum albumins substantially comprising SEQ ID NO:1 or other mutations.

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure

of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

In the instant case it is uncertain what portion of SEQ ID NO:1 should be a part of the mutated human serum albumin as claimed and still retain a function of altered binding activity or function of the native peptide. One skilled in the art cannot ascertain what percent of the SEQ ID NO:1 is incorporated into the mutated albumin since the scope of the word "substantially" is very broad and can mean that the SEQ ID NO:1 is incorporated in its 60% or 75% or 80%. Further, since the substantial identity to the SEQ ID NO:1 is unknown also the function of the mutant is unknown, since Applicant is not in possession of all possible mutations in the human serum albumin, for example. Above all, there is no correlation between the structure and function of the mutated human albumin that substantially comprises SEQ ID NO:1 because any mutant of human serum albumin does not necessary possesses a metal binding affinity or the characteristics of the native serum albumin. Thus, because of the multiplicity of potential mutants there is no correlation between structure and function.

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention i.e. all possible mutated human serum albumins,

where it substantially comprises SEQ ID NO:1, at the time the instant application was filed.

5. Claims 1-10, 13, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the mutant human serum albumin that comprises SEQ ID NO:1, does not reasonably provide enablement for any mutant human serum albumin that substantially comprises SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988*). The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass unspecified proteins i.e. mutant human serum albumins that substantially comprise SEQ ID NO:1, where SEQ ID NO:1 in itself

possess several mutations. Further, there is no binding specify that can be assigned to mutants where the structure of the mutant is unknown. Here, the instant specification does not demonstrate or provide any guidance what would be the structure of a human serum albumin that substantially comprises SEQ ID NO:1 or whether a derivative of such a mutant would exhibit the same characteristics as the native protein. Thus, the experimentation is undue because one skilled in the art must find infinite relevant fragments of SEQ ID NO:1 that have function.

In addition, there is no experimentation that would refer to a disclosure in regards to determination of how one would determine the substantial part of SEQ ID NO:1 that should be included in mutated human serum albumin. Thus, due to the large quantity of experimentation necessary one skilled in the art would not know how to make and use the invention commensurate in scope with the claims.

There is no predictability in regards to which potential changes in the mutant human serum albumin that substantially comprises SEQ ID NO:1 would be conserved and retain the native function of the human serum albumin or a desired metal binding activity. In this case, the necessary guidance was not provided.

Further, the prior art is unpredictable in regards to any mutant serum albumin that substantially possess SEQ ID NO:1, for example.

The state of the prior art provides evidence for the high degree of unpredictability of mutated proteins because of the variability of the protein's structure that can affect its function, for example. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) teach that polypeptides that are identical along relatively long stretches of their

respective sequences exhibit different function. In the instant application, the rejected claims are drawn to any protein, thus the claims would encompass a genus of proteins including their fragments and variants that do not have the same function necessarily.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims in regards to any mutated human serum albumin that substantially comprises SEQ ID NO:1.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed unknown kind or number of mutated human serum albumins that substantially comprise SEQ ID NO:1 because one skilled in the art would have to engage in undue experimentation to compose several mutant that comprise different fragments of SEQ ID NO:1 and see whether the substantially identical fragments to SEQ ID NO:1 have desired function claimed. Thus, one skilled in the art would have to engage in extensive undue experimentation in choosing specially the derived proteins and then examine them for their function.

Therefore, it is clear that the specification does not provide support for the broad scope of the claims that encompass an unspecified number of mutated human serum albumins that substantially comprise SEQ ID NO:1.

Also, absent direction or guidance regarding any mutated human serum albumins that substantially comprise SEQ ID NO:1, one skilled in the art would not be able to practice the claimed invention commensurate in scope with the claims.

Thus, for the aforementioned reasons, the specification is not considered enabling for one skilled in the art to make and use the claimed invention as the amount

of experimentation required is undue, due to the broad scope of the claims regarding any mutated human serum albumins that substantially comprise SEQ ID NO:1, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability. Thus, practicing the method would constitute undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 3, 6-8, 13 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Sargent et al., (Accession No. P02770, 1986, see 892) as evidenced by Andersson et al. (Immobilized metal ion affinity chromatography of serum albumins, Bioseparation 2, pages 15-22, 1991, see 892).

Sargent et al. teach the amino acid sequence of rat serum albumin (RSA) that has 78.3% identity to the human serum albumin (has) (SEQ ID NO:1) of Applicant and thus the RSA substantially comprises SEQ ID NO:1 of Applicant and can be considered a mutant of HSA.

Sargent et al. teach the RSA sequence where in position 242 (the place of mutation designated as X10, according to the instant claims 1 and 8) the residue is N, which is other than H. See the alignment below.

```
ESULT 20
LBU_RAT
D   ALBU_RAT                Reviewed;         608 AA.
C   P02770; P11382; Q5U3X3;
T   21-JUL-1986, integrated into UniProtKB/Swiss-Prot.
T   23-JAN-2007, sequence version 2.
T   21-AUG-2007, entry version 76.
E   Serum albumin precursor.
N   Name=Alb;
S   Rattus norvegicus (Rat).
C   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
C   Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi;
C   Muroidea; Muridae; Murinae; Rattus.
X   NCBI_TaxID=10116;
N   [1]
P   NUCLEOTIDE SEQUENCE [MRNA].
X   MEDLINE=81223722; PubMed=7017712;
A   Sargent T.D., Yang M., Bonner J.;
T   "Nucleotide sequence of cloned rat serum albumin messenger RNA.";
L   Proc. Natl. Acad. Sci. U.S.A. 78:243-246(1981).
N   [2]
P   NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA], AND VARIANT LEU-262.
C   TISSUE=Ovary;
X   PubMed=15489334; DOI=10.1101/gr.2596504;
G   The MGC Project Team;
T   "The status, quality, and expansion of the NIH full-length cDNA
T   project: the Mammalian Gene Collection (MGC).";
L   Genome Res. 14:2121-2127(2004).
N   [3]
P   PROTEIN SEQUENCE OF 1-38, AND PROTEOLYTIC PROCESSING.
X   MEDLINE=77249657; PubMed=893447;
A   Strauss A.W., Bennett C.D., Donohue A.M., Rodkey J.A., Alberts A.W.;
T   "Rat liver pre-proalbumin: complete amino acid sequence of the pre-
T   piece. Analysis of the direct translation product of albumin messenger
T   RNA.";
L   J. Biol. Chem. 252:6846-6855(1977).
N   [4]
P   PROTEIN SEQUENCE OF 25-222.
X   MEDLINE=78109429; PubMed=564345;
```

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  Query Match             78.3%;  Score 2381;  DB 1;  Length 608;
  Best Local Similarity   71.9%;  Pred. No. 1.2e-133;
  Matches  419;  Conservative   93;  Mismatches   71;  Indels    0;  Gaps    0;

Qy          1 DAHKSEVAHRFKDLGEENFKALVLIAFAQXLQQCPFEDHVKLVNEVTEFAKTCVADESAE 60
              :|||||:|||||||||::|| |||||||:|:||:||:|:|:||| |||:||||||||:||
Db         25 EAHKSEIAHRFKDLGEQHFKGLVLIAFSQYLQKCPYEEHIKLVQEVTDFAKTCVADENAE 84

Qy         61 NCDKSLXTLFGDKLCTVATLRETYGEMADCCAKQEPERXXCFXQHKDDNPNLPRLVRPEV 120
              |||||::|||||||| :  ||: |||:||||||||||::||:||||||||||   |||
Db         85 NCDKSIHTLFGDKLCAIPKLRDNYGELADCCAKQEPERNECFLQHKDDNPNLPPFQRPEA 144

Qy        121 DVMCTAFHDNEETFLKKYLYEIARRXPYFYAPELLFFAKRYKAAFTECCQAADKAACLLP 180
              : |||:| :|  :||  ||:|:|||:||||||||::|::|    |:||  :|||||| |
Db        145 EAMCTSFQENPTSFLGHYLHEVARRHPYFYAPELLYYAEKYNEVLTQCCTESDKAACLTP 204

Qy        181 KLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTK 240
              ||| ::::   :: :||:||:|:|:||||||||||||:||||| ||||||:|| ||:||
Db        205 KLDAVKEKALVAAVRQRMKCSSMQRFGERAFKAWAVARMSQRFPNAEFAEITKLATDVTK 264

Qy        241 VXTECCXXXLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSXCIAEVENDEMPA 300
              :: |||:::|||||||||:||||:|||| :|||||: ||:||:|:||:|:||:|:| :||
Db        265 INKECCHGDLLECADDRAELAKYMCENQATISSKLQACCDKPVLQKSQCLAEIEHDNIPA 324

Qy        301 DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKC 360
              ||||:|||||| |:|||||||||||||| |||||:|||||||| ||||||| || |||||
Db        325 DLPSIAADFVEDKEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKC 384

Qy        361 CAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVST 420
              ||  ||  ||  |  ||:||||||:||:| ||||:|:|||| ||||:|||||:| |||||
Db        385 CAEGDPPACYGTVLAEFQPLVEEPKNLVKTNCELYEKLGEYGFQNAVLVRYTQKAPQVST 444

Qy        421 PTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTES 480
              ||||| :||||:||:|||  |||:|:|| ||||| :||:||||||||||::|||||: |
Db        445 PTLVEAARNLGRVGTKCCTLPEAQRLPCVEDYLSAILNRLCVLHEKTPVSEKVTKCCSGS 504

Qy        481 LVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKAT 540
              || |||||||| |||||||||| |||||||:||||| :||:|||||||| ||||||||||
Db        505 LVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLPDKEKQIKKQTALAELVKHKPKAT 564

Qy        541 KEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAAL 583
              ::||| || ||| ||:||||| ||: ||| ||  ||| |: ||
Db        565 EDQLKTVMGDFAQFVDKCCKAADKDNCFATEGPNLVARSKEAL 607
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Moreover, the RSA of Sargent et al. inherently has a different affinity for Ni(II) as evidenced by Andersson et al. Andersson et al. teach immobilized metal ion affinity chromatography of serum albumins and teach that binding of Ni(II), a divalent cation, to an albumin on a column is different in rat (see Figure 2, page 18, that shows two visible picks observed on the "Effluent (ml)" axis) when compared to a binding of Ni(II) to a human albumin (see Figure 3, page 18, that shows only one pick observed on the "Effluent (ml)" axis. Therefore, as evidenced, binding of a divalent cations such as NI(II) and thus also as it would be for Zn(II) is different for rat and human albumin.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have

any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

/Kathleen Kerr Bragdon/

Supervisory Patent Examiner, Art Unit 1656